Medical Expertise

"Development of the European Network in Orphan Cardiovascular Diseases"
„Rozszerzenie Europejskiej Sieci Współpracy ds Sierocych Chorób Kardiologicznych"

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CASE SUMMARY

This is a report of an adult patient with Down syndrome (DS), who presents with a coexistence of Eisenmenger's syndrome and biventricular hypertrophy. Pulmonary hypertension has developed in the course of atrioventricular septal defect (AVSD), which was not corrected in the childhood. He has additional history of hyperthyroidism, currently being in euthyreosis, left-sided hypoacusis, moderate mental retardation and severe dysarthria. On physical examination he shows typical body features of DS, central cyanosis with oxygen saturation ($SatO_2$) of 82%, holosystolic murmur of 3/6 best audible over Erb's point and laud pulmonary component of the second heart sound. 6-minutes walking test (6MWT) reveals severely impaired exercise tolerance and easy fatigue. He reaches distance of 205 meters with prominent desaturation from 82% to 54% at the end of the test and an increase of heart rate from 90 beats per minute (bpm) to 108bpm with unchanged blood pressure of 100/70 mmHg. Laboratory evaluation reveals polycythemia with red blood cells (RBC) of 6,13 mln, hemoglobin (Hb) of 20,33 g/dl and the hematocrit (Hct) of 62,6%. Elevation of NT-proBNP level (1186pg/ml) is observed as well as elevation of uric acid (9,7mg/dl), total cholesterol (292 mg/dl) and urine protein concentration (100mg/dl). 12-lead ECG shows extreme heart axis, regular sinus rhythm and right atrium and ventricle hypertrophy. No particular rhythm or conduction abnormalities are detected on Holter ECG. Echocardiography reveals inlet atrioventricular canal type VSD with bidirectional shunt, double outlet right ventricle, massive hypertrophy of the intraventricular septum (28mm) and right ventricular free wall (16mm). It also shows signs of elevated pulmonary arterial pressure with tricuspid regurgitant jet velocity of 5m/s. Data from the right heart catheterization performed in 2000 show high pulmonary hypertension (PH) with mean pulmonary arterial pressure of 72 mmHg and pulmonary vascular resistance of 12,8 Wood units, mean aortic pressure of 63 mmHg, right-to-left shunt with Qp/Qs ratio of 0,45, low pulmonary and aortic oxygen saturation of 65% and 84%, respectively. No changes in hemodynamic parameters were observed after 10 minutes of 100% oxygen inhalation. On temporal VSD balloon occlusion a deterioration of patients' condition was seen. Patient was qualified for the heart and lung transplantation in 2000, however in 2005 he was rejected from the waiting list due to his parents decision. He was treated with digoxin, nifedipine and home oxygen and since 2010 sildenafil and arginine was added. The authors are hesitant with regards to the etiology of the biventricular hypertrophy, further treatment strategy and the indications for the cardioverter defibrillator

implantation.

DISCUSSION

Trisomy 21 is one of the most common chromosomal anomaly observed in approximately 1 out of 800 live births [1]. Its prevalence raises with the age of the mother being as frequent as 1:100 live births in 40 year-old females. No sex or race differences have been reported. DS is characterized by a variety of dysmorphic features, congenital malformations, and other health problems and medical conditions. Among frequently observed findings like duodenal atresia or stenosis, obesity, vision problems, hearing loss, thyroid disease, diabetes, leukemias or urological abnormalities, disorders of the heart are seen in as many as a half of DS patients [2]. Most prevalent, complete AVSD, is detected in approximately 37% of cases [2]. It is a result of impaired development of endocardial cushions. One fourth of DS patients may have more than on defect. These include isolated ventricular septal defect (VSD), atrial septal defect (ASD), tetralogy of Fallot (ToF), patent ductus arteriosus (PDA) or heterotaxy syndrome.

Pathophysiologically AVSDs results in increased pulmonary blood flow because of left-to-right shunting at the atrial and ventricular levels. If uncorrected, an excessive pulmonary blood flow leads to elevation of pulmonary vascular resistance and pulmonary artery hypertension (PAH). Eventually, the progression of pulmonary vascular disease leads to irreversible PH, presenting with systemic oxygen desaturation and cyanosis due to right-to-left shunting – the Eisenmenger syndrome.

Definite treatment of the AVSDs is surgical and is performed in infancy.

As long as pulmonary hypertension and Eisenmenger syndrome occurs commonly in DS patients with congenital intracardiac shunts, coexistence of hypertrophic cardiomyopathy (HCM) is rather a rare finding in this group of patients. There is a few reports describing cases of DS patients, who have AVSD complicated by pulmonary hypertension and hypertrophic cardiomyopathy [3,4].

EXPERT'S OPINION

This is an example of PAH associated with congenital heart disease (CHD), namely AVSD – group 1 of the PH clinical classification. Considering his clinical status, he would be classified as having markedly limited normal physical capacity - functional class III by WHO [5]. A short distance achieved on 6MWT, significant desaturation seen at the end of the test, high NT-proBNP level, erythrocytosis expresses poor prognosis for this patient and urge reevaluation of the current treatment.

- According to the guidelines [5] adding endothelin receptor antagonist (ERA) should be advised at this point. In case of further deterioration additional treatment with prostacyclin is also applicable.

- "The use of supplemental O2 therapy should be considered if it produces a consistent increase in arterial oxygen saturation and reduces symptoms.", although no convincing data are available on O2 supplementation in Eisenmenger's patients.

- Calcium channel blockers are not indicated in Eisenmenger's syndrome, therefore discontinuation of nifedipine should be advised, especially in this case with relatively low blood pressure.

- Digoxin has been used for a long time now. It is however unknown whether any

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rhythm abnormalities were ever detected in this patient. Continuous monitoring of ecg does not reveal any rhythm or conduction abnormalities at the moment. Monitoring of the digoxin blood concentration should be recommended. Digoxin is not recommended in hypertrophic cardiomyopathy with LV outflow tract obstruction. The need for further use of digoxin should be reevaluated.

- According to the guidelines, phlebotomy is indicated in case of symptoms of hyperviscosity syndrome and haematocrit of 65%. Detailed consideration should be conducted before deciding for phlebotomy. Nevertheless, diuretic agents should be used with caution not to increase the viscosity of the blood.

Presence of biventricular hypertrophy in this patient, especially affecting IVS is suggestive for the diagnosis of HCM. Isolated HCM is genetically or metabolically determined condition, which is very rarely described in DS patients with congenital cardiac shunts. Genetic background for the combination of HCM and AVSD in DS patients have been proposed, but no evidences have been found so far [3] On the other hand, RV hypertrophy is a typical consequence of PH and is often seen in PH patients with DS. Long-lasting bidirectional shunting may result in LV volumic and pressure overload and lead to hypertrophy. No resources seem to be available now to determine what is the actual cause of the observed LV hypertrophy in this patient.

- There is no family history of sudden cardiac death, no ventricular arrhythmia or unexpected syncope has been reported in this patient. The risk of thromboembolic complication on the other hand, when inserting intracardiac electrodes is higher in Eisenmenger's patients, thus an ICD is no recommended.

CONCLUSION

Otpimization of PH specific therapy is recommended. Close follow – up with regular echocardiography and 6MWT, every 6 months seems reasonable. No ICD is recommended.

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